EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
.L1	332	DMXAA	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2006/11/08 09:35
L2	4279	gemcitabine	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2006/11/08 09:35
L3	67	L1 L2	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	OFF	2006/11/08 09:47
L4	45498	wilson.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	OFF	2006/11/08 09:36
L5	. 7	L1 L4	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	OFF	2006/11/08 09:36
L6	2	l1 l2	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	NEAR	OFF [*]	2006/11/08 09:47

FILE 'HOME' ENTERED AT 09:12:12 ON 08 NOV 2006

=> file medline, caplus, wpids, uspatfull

=> s "DMXAA" or "5,6-dimethyl-xanthenone-4 acetic acid"

538 "DMXAA" OR "5,6-DIMETHYL-XANTHENONE-4 ACETIC ACID" L1

=> s "gemcitabine"

11744 "GEMCITABINE" L2

=> s "vascular targeting agent?"

229 "VASCULAR TARGETING AGENT?"

=> s "solid tumor?"

16897 "SOLID TUMOR?"

=> s 11 and 12

71 L1 AND L2

=> s 12 and 13

43 L2 AND L3

=> s 15 and 14

L7 38 L5 AND L4

=> s 11 and 12 and 13

23 L1 AND L2 AND L3

=> s 18 and 14

Ь9 19 L8 AND L4

=> s 15 not py>2001

L10 0 L5 NOT PY>2001

=> s 16 not py>2001

0 L6 NOT PY>2001 L11

=> s 17 not py>2001

L12 0 L7 NOT PY>2001

=> s 15 not py>2002

1 L5 NOT PY>2002

=> d 113 ibib, abs

L13 ANSWER 1 OF 1 USPATFULL on STN

ACCESSION NUMBER:

2002:213736 USPATFULL Full-text

TITLE:

INVENTOR (S):

Neutrokine-alpha and Neutrokine-alpha splice variant

Yu, Guo-Liang, Berkeley, CA, UNITED STATES

Ebner, Reinhard, Gaithersburg, MD, UNITED STATES Ni, Jian, Germantown, MD, UNITED STATES

Rosen, Craig A., Laytonsville, MD, UNITED STATES Ullrich, Stephen, Rockville, MD, UNITED STATES

PATENT ASSIGNEE(S):

Human Genome Sciences, Inc., Rockville, MD, UNITED

STATES, 20850 (U.S. corporation)

	NUMBER	KIND	DATE	
	·			
PATENT INFORMATION:	US 2002115112	A1	20020822	
APPLICATION INFO.:	US 2001-929493	A1	20010815	(9)

RELATED APPLN. INFO.:

Continuation-in-part of Ser. No. US 2000-588947, filed on 8 Jun 2000, PENDING Continuation-in-part of Ser. No. US 2000-589285, filed on 8 Jun 2000, PENDING Continuation-in-part of Ser. No. US 2000-589286, filed on 8 Jun 2000, PENDING Continuation-in-part of Ser. No. US 2000-589287, filed on 8 Jun 2000, PENDING Continuation-in-part of Ser. No. US 2000-586288, filed on 2 Jun 2000, PATENTED Continuation-in-part of Ser. No. US 2000-507968, filed on 22 Feb 2000, PENDING Continuation-in-part of Ser. No. US 1999-255794, filed on 23 Feb 1999, PENDING Continuation-in-part of Ser. No. US 1999-255794, filed on 23 Feb 1999, PENDING

			NUMBER	DATE	
PRIORITY I	NFORMATION:	US	2000-225628P	20000815	(60)
•		US	2000-227008P	20000823	(60)
		US	2000-234338P	20000922	(60)
		US	2000-240806P	20001017	(60)
•		US	2000-250020P	20001130	(60)
		US	2001-276248P	20010316	(60)
		US	2001-293499P	20010525	(60)
		US	2001-296122P	20010607	(60)
		US	2001-304809P	20010713	(60)
	•	US	1999-122388P	19990302	(60)
		US	1999-124097P	19990312	(60)
		US	1999-126599P	19990326	(60)
		US	1999-127598P	19990402	(60)
		US	1999-130412P	19990416	(60)
		US	1999-130696P	19990423	(60)
		US	1999-131278P	19990427	(60)
		US	1999-131673P	19990429	(60)
		US	1999-136784P	19990528	(60)
		US	1999-142659P	19990706	(60)
		US	1999-145824P	19990727	(60)
•		US	1999-167239P	19991124	(60)
		US	1999-168624P	19991203	(60)
		US	1999-171108P	19991216	(60)
		US	1999-171626P	19991223	(60)
		US	2000-176015P	20000114	(60)
DOCUMENT T	YPE:	Ut:	ility		

FILE SEGMENT: Offiley

APPLICATION

LEGAL REPRESENTATIVE: HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE,

ROCKVILLE, MD, 20850

NUMBER OF CLAIMS: 117 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 22 Drawing Page(s)

LINE COUNT: 18178

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention relates to nucleic acid molecules encoding Neutrokine-alpha and/or Neutrokine-alphaSV polypeptides, including soluble forms of the extracellular domain. Neutrokine-alpha and/or Neutrokine-alphaSV polypeptides are also provided as are vectors, host cells and recombinant methods for producing the same. The invention further relates to antibodies or portions thereof that specifically bind Neutrokine-alpha and/or Neutrokine-alphaSV and diagnostic and therapeutic methods using these antibodies. Also provided are diagnostic methods for detecting immune system-related disorders and therapeutic methods for treating immune system-related disorders using the compositions of the invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 19 1-19 ibib, abs

ANSWER 1 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2006:267618 USPATFULL Full-text

TITLE: Constructs binding to phosphatidylserine and their use

in disease treatment

INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES

Luster, Troy A., Dallas, TX, UNITED STATES

King, Steven W., Ladera Ranch, CA, UNITED STATES

PATENT ASSIGNEE(S): Board of Regents, The University of Texas System (U.S.

corporation)

Peregrine Pharmaceuticals, Inc. (U.S. corporation)

NUMBER KIND DATE -----PATENT INFORMATION: APPLICATION INFO.: US 2006228299 A1 20061012 US 2006-339392 A1 20060124 (11)

NUMBER DATE ·----

PRIORITY INFORMATION: US 2005-646333P 20050124 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: PEREGRINE PHARMACEUTICALS, INC., 5353 WEST ALABAMA,

SUITE 306, HOUSTON, TX, 77056, US

NUMBER OF CLAIMS: EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 28 Drawing Page(s)

LINE COUNT: 12525

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Disclosed are new phosphatidylserine binding constructs with surprising combinations of properties, and a range of diagnostic and therapeutic conjugates thereof. The new constructs effectively bind phosphatidylserine targets in disease and enhance their destruction, and can also specifically deliver attached imaging or therapeutic agents to the disease site. Also disclosed are methods of using the new construct compositions, therapeutic conjugates and combinations thereof in tumor vasculature targeting, cancer diagnosis and treatment, and for treating viral infections and other diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 2 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2005:157851 USPATFULL Full-text

TITLE: Cancer treatment methods using selected antibodies to

aminophospholipids

INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES

Ran, Sophia, Riverton, IL, UNITED STATES

NUMBER KIND DATE -----PATENT INFORMATION: US 2005136059 A1 20050623 US 2003-642071 A1 20030815 (10) APPLICATION INFO.:

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2003-621269, filed

on 15 Jul 2003, PENDING

NUMBER DATE -----

PRIORITY INFORMATION: US 2002-396263P 20020715 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: WILLIAMS, MORGAN & AMERSON, P.C., 10333 RICHMOND, SUITE

1100, HOUSTON, TX, 77042, US

NUMBER OF CLAIMS: 20 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 53 Drawing Page(s)

LINE COUNT: 13044

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 3 OF 19 USPATFULL on STN L9

ACCESSION NUMBER: 2005:150785 USPATFULL Full-text

TITLE: Cancer treatment methods using selected

immunoconjugates for binding to aminophospholipids

INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES

Ran, Sophia, Riverton, IL, UNITED STATES

NUMBER KIND DATE US 2005129696 A1 20050616

US 2005129696 A1 US 2003-642065 A1 APPLICATION INFO.: 20030815 (10)

Continuation-in-part of Ser. No. US 2003-621269, filed RELATED APPLN. INFO.:

on 15 Jul 2003, PENDING

NUMBER DATE -----

PRIORITY INFORMATION: US 2002-396263P 20020715 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: WILLIAMS, MORGAN & AMERSON, P.C., 10333 RICHMOND, SUITE

1100, HOUSTON, TX, 77042, US

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

PATENT INFORMATION:

NUMBER OF DRAWINGS: 53 Drawing Page(s)

LINE COUNT: 13046

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 4 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2005:69437 USPATFULL Full-text

TITLE: Compositions comprising phosphatidylethanolamine-

> binding peptides linked to anti-viral agents Thorpe, Philip E., Dallas, TX, UNITED STATES Soares, M. Melina, Richardson, TX, UNITED STATES

He, Jin, Dallas, TX, UNITED STATES

NUMBER KIND DATE

-----PATENT INFORMATION:

US 2005059578 A1 20050317 US 2003-642121 A1 20030815 (10) APPLICATION INFO.:

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2003-621269, filed

on 15 Jul 2003, PENDING

NUMBER DATE -----

PRIORITY INFORMATION: US 2002-396263P 20020715 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: WILLIAMS, MORGAN & AMERSON, P.C., 10333 RICHMOND, SUITE

1100, HOUSTON, TX, 77042

NUMBER OF CLAIMS: 21 EXEMPLARY CLAIM:

INVENTOR(S):

NUMBER OF DRAWINGS: 53 Drawing Page(s)

LINE COUNT: 13308

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 5 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2005:36945 USPATFULL Full-text

TITLE: Combined cancer treatment methods using selected

antibodies to aminophospholipids

INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES

Huang, Xianming, Dallas, TX, UNITED STATES Ran, Sophia, Riverton, IL, UNITED STATES

NUMBER KIND DATE -----PATENT INFORMATION: US 2005031620 A1 20050210 APPLICATION INFO.: US 2003-642058 A1 20030815 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2003-621269, filed

on 15 Jul 2003, PENDING

NUMBER DATE -----

PRIORITY INFORMATION: US 2002-396263P 20020715 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: WILLIAMS, MORGAN & AMERSON, P.C., 10333 RICHMOND, SUITE

1100, HOUSTON, TX, 77042

NUMBER OF CLAIMS: 3 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 53 Drawing Page(s)

LINE COUNT: 13439

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 6 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2005:30331 USPATFULL <u>Full-text</u>
TITLE: Anti-viral treatment methods using

phosphatidylethanolamine-binding peptides linked to

anti-viral agents

INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES

Soares, M. Melina, Richardson, TX, UNITED STATES

He, Jin, Dallas, TX, UNITED STATES

PATENT ASSIGNEE(S): Board of Regents, The University of Texas System (U.S.

corporation)

APPLICATION INFO.: US 2003-642100 A1 20030815 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2003-621269, filed

on 15 Jul 2003, PENDING

NUMBER DATE

PRIORITY INFORMATION: US 2002-396263P 20020715 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: WILLIAMS, MORGAN & AMERSON, P.C., 10333 RICHMOND, SUITE

1100, HOUSTON, TX, 77042

NUMBER OF CLAIMS: 23 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 52 Drawing Page(s)

LINE COUNT: 13426

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 7 OF 19 USPATFULL on STN

2005:3839 USPATFULL Full-text ACCESSION NUMBER:

TITLE: Combinations and kits for cancer treatment using

selected antibodies to aminophospholipids INVENTOR (S): Thorpe, Philip E., Dallas, TX, UNITED STATES

Huang, Xianming, Dallas, TX, UNITED STATES

Ran, Sophia, Riverton, IL, UNITED STATES

Board of Regents, The University of Texas System (U.S. PATENT ASSIGNEE(S):

corporation)

NUMBER KIND DATE -----

US 2005002941 A1 20050106 US 2003-642116 A1 20030815 (10) PATENT INFORMATION:

APPLICATION INFO.:

Continuation-in-part of Ser. No. US 2003-621269, filed RELATED APPLN. INFO.:

on 15 Jul 2003, PENDING

NUMBER -----

PRIORITY INFORMATION: US 2002-396263P 20020715 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: WILLIAMS, MORGAN & AMERSON, P.C., 10333 RICHMOND, SUITE

1100, HOUSTON, TX, 77042

NUMBER OF CLAIMS: 28 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 53 Drawing Page(s)

LINE COUNT: 13468

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Disclosed are surprising discoveries concerning the role of anionic ABphospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 8 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2004:334289 USPATFULL Full-text

TITLE: Liposomes coated with selected antibodies that bind to

aminophospholipids

INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES

Huang, Xianming, Dallas, TX, UNITED STATES Ran, Sophia, Riverton, IL, UNITED STATES

NUMBER KIND DATE -----US 2004265367 PATENT INFORMATION: 20041230

A1 US 2003-642064 A1 APPLICATION INFO.: 20030815 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2003-621269, filed

on 15 Jul 2003, PENDING

NUMBER DATE

-----US 2002-396263P 20020715 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: WILLIAMS, MORGAN & AMERSON, P.C., 10333 RICHMOND, SUITE

1100, HOUSTON, TX, 77042

NUMBER OF CLAIMS: 23 EXEMPLARY CLAIM:

PRIORITY INFORMATION:

NUMBER OF DRAWINGS: 53 Drawing Page(s)

LINE COUNT: 13511

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycinbased compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 9 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2004:279855 USPATFULL Full-text

TITLE: Selected immunoconjugates for binding to

aminophospholipids

INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES

Ran, Sophia, Riverton, IL, UNITED STATES

NUMBER KIND DATE -----US 2004219155 A1 20041104 US 2003-642099 A1 20030815 (10)

APPLICATION INFO.:

Continuation-in-part of Ser. No. US 2003-621269, filed RELATED APPLN. INFO.:

on 15 Jul 2003, PENDING

DATE NUMBER -----

PRIORITY INFORMATION: US 2002-396263P 20020715 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

Shelley P.M. Fussey, Williams, Morgan & Amerson, P.C., LEGAL REPRESENTATIVE:

Suite 1100, 10333 Richmond, Houston, TX, 77042

NUMBER OF CLAIMS: 31 EXEMPLARY CLAIM: 1

PATENT INFORMATION:

NUMBER OF DRAWINGS: 53 Drawing Page(s)

LINE COUNT: 13474

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

ANSWER 10 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2004:274262 USPATFULL Full-text

TITLE: Anti-viral treatment methods using

phosphatidylethanolamine-binding peptide derivatives

Thorpe, Philip E., Dallas, TX, UNITED STATES INVENTOR(S):

Soares, M. Melina, Richardson, TX, UNITED STATES

He, Jin, Dallas, TX, UNITED STATES

NUMBER KIND

PATENT INFORMATION: -----

US 2004214764 A1 20041028 US 2003-642117 A1 20030815 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2003-621269, filed

on 15 Jul 2003, PENDING

NUMBER DATE -----

US 2002-396263P 20020715 (60) PRIORITY INFORMATION:

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Shelley P.M. Fussey, WILLIAMS, MORGAN & AMERSON, P.C.,

Suite 1100, 10333 Richmond, Houston, TX, 77042

NUMBER OF CLAIMS: EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 53 Drawing Page(s)

LINE COUNT: 13426

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ΔR Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 11 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2004:273287 USPATFULL Full-text

TITLE: Methods for treating viral infections using

immunoconjugates to aminophospholipids

INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES

Soares, M. Melina, Richardson, TX, UNITED STATES

Ran, Sophia, Riverton, IL, UNITED STATES

NUMBER KIND -----US 2004213779 A1 20041028 US 2003-642119 A1 20030815 (10)

PATENT INFORMATION: APPLICATION INFO.:

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2003-621269, filed

on 15 Jul 2003, PENDING

NUMBER DATE -----

PRIORITY INFORMATION: US 2002-396263P 20020715 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION LEGAL REPRESENTATIVE: Shelley P.M. Fussey, Williams, Morgan & Amerson, P.C.,

Suite 1100, 10333 Richmond, Houston, TX, 77042

NUMBER OF CLAIMS: 31 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 53 Drawing Page(s)

LINE COUNT: 13438

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 12 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2004:267331 USPATFULL Full-text TITLE: Selected antibody CDRs for binding to

aminophospholipids

INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES

Ran, Sophia, Riverton, IL, UNITED STATES

PATENT ASSIGNEE(S): Board of Regents, The University of Texas System (U.S.

corporation)

NUMBER KIND DATE -----US 2004208868 A1 20041021 US 2003-642118 A1 20030815 (10)

APPLICATION INFO.:

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2003-621269, filed

on 15 Jul 2003, PENDING

NUMBER DATE ·----

US 2002-396263P 20020715 (60) PRIORITY INFORMATION:

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Shelley P.M. Fussey, Williams,, Morgan & Amerson, P.C.,

10333 Richmond, Suite 1100, Houston, TX, 77042

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

PATENT INFORMATION:

NUMBER OF DRAWINGS: 53 Drawing Page(s)

LINE COUNT: 13435

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2004:226993 USPATFULL Full-text

TITLE: Selected antibody compositions and methods for binding

to aminophospholipids

INVENTOR (S): Thorpe, Philip E., Dallas, TX, UNITED STATES

Ran, Sophia, Riverton, IL, UNITED STATES

Board of Regents, The University of Texas System (U.S. PATENT ASSIGNEE(S):

corporation)

NUMBER KIND DATE -----

US 2004175378 A1 20040909 US 2003-620850 A1 20030715 PATENT INFORMATION:

A1 APPLICATION INFO.: 20030715 (10)

NUMBER DATE

PRIORITY INFORMATION: US 2002-396263P 20020715 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Shelley P.M. Fussey, Williams, Morgan & Amerson, P.C.,

Suite 1100, 10333 Richmond, Houston, TX, 77042

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 53 Drawing Page(s)

LINE COUNT: 12773

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related

diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 14 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2004:220853 USPATFULL Full-text

TITLE: Selected antibody compositions for binding to

aminophospholipids

INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES

Ran, Sophia, Riverton, IL, UNITED STATES

KIND NUMBER DATE -----US 2004170620 A1 20040902 US 2003-621269 A1 20030715 (10) US 2004170620 PATENT INFORMATION: APPLICATION INFO.:

NUMBER DATE -**----**

PRIORITY INFORMATION: US 2002-396263P 20020715 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Shelley P.M. Fussey, Williams, Morgan & Amerson, P.C.,

Suite 1100, 10333 Richmond, Houston, TX, 77042

NUMBER OF CLAIMS: 92 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 53 Drawing Page(s)

LINE COUNT: 13072 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 15 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2004:208997 USPATFULL Full-text

TITLE: Compositions for treating viral infections using

immunoconjugates to aminophospholipids

INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES

Soares, M. Melina, Richardson, TX, UNITED STATES

Ran, Sophia, Riverton, IL, UNITED STATES

NUMBER KIND DATE

PATENT INFORMATION: US 2004161429 A1 20040819

APPLICATION INFO.: US 2003-642124 A1 20030815 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2003-621269, filed

on 15 Jul 2003, PENDING

NUMBER DATE

PRIORITY INFORMATION: US 2002-396263P 20020715 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: WILLIAMS, MORGAN & AMERSON, P.C., 10333 RICHMOND, SUITE

1100, HOUSTON, TX, 77042

NUMBER OF CLAIMS: 22 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 53 Drawing Page(s)

LINE COUNT: 13334

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycinbased compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 16 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2004:190667 USPATFULL Full-text

TITLE: Compositions comprising cell-impermeant duramycin

derivatives

INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES

He, Jin, Dallas, TX, UNITED STATES

PATENT ASSIGNEE(S): Board of Regents, The University of Texas System (U.S.

corporation)

NUMBER KIND DATE ----- -----

PATENT INFORMATION: US 2004147440 A1 US 2004147440 A1 US 2003-642059 A1 20040729

APPLICATION INFO.: 20030815 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2003-621269, filed

on 15 Jul 2003, PENDING

NUMBER DATE -----

US 2002-396263P 20020715 (60) PRIORITY INFORMATION:

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Shelley P.M. Fussey, WILLIAMS, MORGAN & AMERSON, P.C.,

Suite 1100, 10333 Richmond, Houston, TX, 77042

NUMBER OF CLAIMS: EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 53 Drawing Page(s)

LINE COUNT: 13402

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 17 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2004:171463 USPATFULL Full-text

TITLE: Combinations and kits for treating viral infections

using immunoconjugates to aminophospholipids

INVENTOR (S): Thorpe, Philip E., Dallas, TX, UNITED STATES

Soares, M. Melina, Richardson, TX, UNITED STATES

Ran, Sophia, Riverton, IL, UNITED STATES

PATENT ASSIGNEE(S): Board of Regents (U.S. corporation)

The University of Texas System (U.S. corporation)

NUMBER KIND DATE US 2004131622 A1 20040708 PATENT INFORMATION:

US 2003-642122 A1 APPLICATION INFO.: 20030815 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2003-621269, filed

on 15 Jul 2003, PENDING

NUMBER DATE -----

PRIORITY INFORMATION: US 2002-396263P 20020715 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Shelley P.M. Fussey, Williams, Morgan & Amerson, P.C.,

Suite 1100, 10333 Richmond, Houston, TX, 77042

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 53 Drawing Page(s)

LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 'ANSWER 18 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2004:171462 USPATFULL Full-text

TITLE: Combinations and kits for treating viral infections

using antibodies to aminophospholipids

INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES

Soares, M. Melina, Richardson, TX, UNITED STATES

Ran, Sophia, Riverton, IL, UNITED STATES

NUMBER KIND DATE

PATENT INFORMATION: US 2004131621 A1 20040708

APPLICATION INFO.: US 2003-642060 A1 20030815 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2003-621269, filed

on 15 Jul 2003, PENDING

NUMBER DATE

PRIORITY INFORMATION: US 2002-396263P 20020715 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Shelley P.M. Fussey, Williams, Morgan & Amerson, P.C.,

Suite 1100, 10333 Richmond, Houston, TX, 77042

NUMBER OF CLAIMS: 23 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 53 Drawing Page(s)

LINE COUNT: 13167

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 19 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2004:171451 USPATFULL Full-text

TITLE: Methods for treating viral infections using antibodies

to aminophospholipids

INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES

Soares, M. Melina, Richardson, TX, UNITED STATES

Ran, Sophia, Riverton, IL, UNITED STATES

NUMBER KIND DATE -----

PATENT INFORMATION:

US 2004131610 A1 20040708 US 2003-642120 A1 20030815 (10) APPLICATION INFO.:

Continuation-in-part of Ser. No. US 2003-621269, filed RELATED APPLN. INFO.:

on 15 Jul 2003, PENDING

NUMBER

US 2002-396263P 20020715 (60) PRIORITY INFORMATION:

DOCUMENT TYPE: Utility APPLICATION FILE SEGMENT:

LEGAL REPRESENTATIVE: Shelley P.M. Fussey, Williams, Morgan & Amerson, P.C.,

Suite 1100, 10333 Richmond, Houston, TX, 77042

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 53 Drawing Page(s)

LINE COUNT: 13359

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his

(FILE 'HOME' ENTERED AT 09:12:12 ON 08 NOV 2006)

FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 09:12:35 ON 08 NOV 2006

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L1
           538 S "DMXAA" OR "5,6-DIMETHYL-XANTHENONE-4 ACETIC ACID"
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L2 11744 S "GEMCITABINE"

229 S "VASCULAR TARGETING AGENT?" L3

L416897 S "SOLID TUMOR?"

L5 71 S L1 AND L2

L6 43 S L2 AND L3 L7 38 S L5 AND L4

L823 S L1 AND L2 AND L3

L9 19 S L8 AND L4

L10 0 S L5 NOT PY>2001 0 S L6 NOT PY>2001 L11

L120 S L7 NOT PY>2001

L13 1 S L5 NOT PY>2002

=> s "synergistic"

170074 "SYNERGISTIC"

=> s 12 and 114

L15 1514 L2 AND L14

=> d his

(FILE 'HOME' ENTERED AT 09:12:12 ON 08 NOV 2006)

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FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 09:12:35 ON 08 NOV
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L2
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            229 S "VASCULAR TARGETING AGENT?"
L3
L4
          16897 S "SOLID TUMOR?"
L5
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L6
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L15
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=> s 16 not py>2002
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2 L6 NOT PY>2002

=> d 116 1-2 ibib, abs

L16 ANSWER 1 OF 2 MEDLINE on STN

ACCESSION NUMBER: 2002698167 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 12459376

TITLE:

The development of combretastatin A4 phosphate as a

vascular targeting agent.

AUTHOR: Chaplin David J; Hill Sally A

CORPORATE SOURCE: Oxigene Inc., Watertown, MA 02472, USA..

dchaplin@oxigene.com

SOURCE: International journal of radiation oncology, biology,

physics, (2002 Dec 1) Vol. 54, No. 5, pp. 1491-6.

Journal code: 7603616. ISSN: 0360-3016.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE) DOCUMENT TYPE:

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200301

AB

ENTRY DATE: Entered STN: 17 Dec 2002

> Last Updated on STN: 3 Jan 2003 Entered Medline: 2 Jan 2003

depolymerizing agents as vascular targeting agents, leading to the identification of combretastatin A4P (CA4P). Methods and Materials: The murine tumor CaNT was implanted s.c. in the dorsum of CBA mice. Vascular function was determined after treatment using the perfusion marker Hoechst 33342 and fluorescence microscopy. Tumor cell response was assessed by using an excision assay and by measuring the delay in growth of treated tumors. Results: At doses that approximated one-half the maximum tolerated dose (MTD) in CBA mice, none of the agents evaluated-i.e., taxol, melphalan, 5-fluorouracil, doxorubicin, cisplatin, gemcitabine, and irinotecan-induced any significant reduction in perfused vascular volume within the tumor mass. In contrast, CA4P at a dose of 100 mg/kg, which approximates one-fifth the MTD, induced a greater than 80% reduction in vascular function. Although colchicine did

induce vascular shutdown, this occurred only at doses approximating the MTD. Histologic evaluation demonstrated that continued growth and repopulation of the tumor mass was the result of a surviving rim of viable tumor cells at the

Purpose: This overview summarizes the preclinical development of tubulin-

tumor periphery Conclusion: These results confirm the ability of CA4P to selectively compromise vascular function in experimental tumors, inducing extensive tumor cell death at well-tolerated doses. However, despite these effects, no growth retardation is obtained when CA4P is administered alone in a single dose. The continued growth and repopulation of the tumor mass occurs from a narrow rim of viable cells at the periphery. If, as is believed, these remaining cells are the ones most sensitive to conventional cytotoxic and macromolecular approaches, CA4P and other vascular targeting agents offer considerable potential for enhancing the effectiveness of existing and emerging cancer therapies.

L16 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:896034 CAPLUS Full-text

DOCUMENT NUMBER: 139:316714

TITLE: The development of combretastatin A4 phosphate as a

vascular targeting agent

AUTHOR(S): Chaplin, David J.; Hill, Sally A.

CORPORATE SOURCE: Oxigene Inc., Watertown, MA, 02472, USA

SOURCE: International Journal of Radiation Oncology, Biology,

Physics (2002), 54(5), 1491-1496 CODEN: IOBPD3; ISSN: 0360-3016

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal LANGUAGE: English

Purpose: This overview summarizes the preclin. development of tubulin-AB depolymg. agents as vascular targeting agents, leading to the identification of combretastatin A4P (CA4P). Methods and Materials: The murine tumor CaNT was implanted s.c. in the dorsum of CBA mice. Vascular function was determined after treatment using the perfusion marker Hoechst 33342 and fluorescence microscopy. Tumor cell response was assessed by using an excision assay and by measuring the delay in growth of treated tumors. Results: At doses that approximated one-half the maximum tolerated dose (MTD) in CBA mice, none of the agents evaluated-i.e., taxol, melphalan, 5fluorouracil, doxorubicin, cisplatin, gemcitabine, and irinotecan-induced any significant reduction in perfused vascular volume within the tumor mass. In contrast, CA4P at a dose of 100 mg/kg, which approximates one-fifth the MTD, induced a greater than 80% reduction in vascular function. Although colchicine did induce vascular shutdown, this occurred only at doses approximating the MTD. Histol. evaluation demonstrated that continued growth and repopulation of the tumor mass was the result of a surviving rim of viable tumor cells at the tumor periphery. Conclusion: These results confirm the ability of CA4P to selectively compromise vascular function in exptl. tumors, inducing extensive tumor cell death at well-tolerated doses. However, despite these effects, no growth retardation is obtained when CA4P is administered alone in a single dose. The continued growth and repopulation of the tumor mass occurs from a narrow rim of viable cells at the periphery. If, as is believed, these remaining cells are the ones most sensitive to conventional cytotoxic and macromol. approaches, CA4P and other vascular targeting agents offer considerable potential for enhancing the effectiveness of existing and emerging cancer therapies.

REFERENCE COUNT:

THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'HOME' ENTERED AT 09:12:12 ON 08 NOV 2006)

37

FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 09:12:35 ON 08 NOV

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L2
         11744 S "GEMCITABINE"
L3
           229 S "VASCULAR TARGETING AGENT?"
         16897 S "SOLID TUMOR?"
L4
L5
            71 S L1 AND L2
L6
            43 S L2 AND L3
L7
            38 S L5 AND L4
L8
            23 S L1 AND L2 AND L3
            19 S L8 AND L4
L9
             0 S L5 NOT PY>2001
L10
             0 S L6 NOT PY>2001
L11
L12
             0 S L7 NOT PY>2001
L13
             1 S L5 NOT PY>2002
L14
       170074 S "SYNERGISTIC"
L15
          1514 S L2 AND L14
L16
             2 S L6 NOT PY>2002
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=>

⁻⁻⁻Logging off of STN---

10/790,943 - STRUCTURE SEARCH

FILE 'HOME' ENTERED AT 09:28:31 ON 08 NOV 2006

=> file registry

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Uploading C:\Program Files\Stnexp\Queries\10790943str.str

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ring nodes :
1 2 3 4 5 6 7
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chain bonds :
4-15 7-25 8-26 9-27 10-18 11-16 12-17 13-23 14-24 18-19 18-28 18-29 19-
20
19-21
ring bonds :
1-2 1-6 2-3 2-11 3-4 3-14 4-5 5-6 5-7 6-10 7-8 8-9 9-10 11-12 12-13
exact/norm bonds :
4-15
exact bonds :
1-2 1-6 3-4 4-5 7-25 8-26 9-27 10-18 11-16 12-17 13-23 14-24 18-19 18-
28
18-29
normalized bonds :
2-3 2-11 3-14 5-6 5-7 6-10 7-8 8-9 9-10 11-12 12-13 13-14 19-20 19-21
isolated ring systems :
containing 1 :
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Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom '9:Atom 10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS

L1 STRUCTURE UPLOADED

=> d 11

L1 HAS NO ANSWERS

Structure attributes must be viewed using STN Express query preparation.

=> s 11

SAMPLE SEARCH INITIATED 09:29:13 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED -4 TO ITERATE

100.0% PROCESSED

4 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 4 TO 200

PROJECTED ANSWERS:

0 TO

L2 0 SEA SSS SAM L1

=> s l1 exa full

FULL SEARCH INITIATED 09:29:21 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED -6 TO ITERATE

100.0% PROCESSED 6 ITERATIONS 1 ANSWERS

SEARCH TIME: 00.00.01

L3 1 SEA EXA FUL L1

=> d scan

1 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN L3

IN 9H-Xanthene-4-acetic acid, 5,6-dimethyl-9-oxo- (9CI)

MF C17 H14 O4

CI COM

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=> file medline, caplus, wpids, uspatfull

=> s 13

SAMPLE SEARCH INITIATED 09:29:47 FILE 'WPIDS'

SAMPLE SCREEN SEARCH COMPLETED -

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100.0% PROCESSED

0 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

0 TO

PROJECTED ITERATIONS:

0 TO

PROJECTED ANSWERS:

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L5 7 L4 AND "GEMCITABINE"

=> d 15 1-7 ibib, abs, hitstr

L5 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2005:984120 CAPLUS Full-text

DOCUMENT NUMBER:

143:279360

TITLE:

Methods of detecting CD133 antigen (AC133) expression

level and use as biomarker for human cancer diagnosis

and therapy monitor

INVENTOR(S):

Penning, Maarten Tjerk; Van den Broek, Sebastiaan

Johannes Jacobus; Voest, Emile Eugene; Beerepoot,

Laurens Victor; Mehra, Niven

PATENT ASSIGNEE (S):

Primagen Holding B. V., Neth.; UMC Utrecht Holding B.

٧.

SOURCE:

PCT Int. Appl., 55 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2005083123 A1 20050909 WO 2005-NL155 20050302

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG EP 1571225 A1 20050907 EP 2004-75686 20040302 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK 20050909 · AA CA 2005-2558604 PRIORITY APPLN. INFO.: EP 2004-75686 A 20040302 US 2004-549450P P 20040302 WO 2005-NL155 W 20050302

This invention provides methods of detecting CD133 antigen (AC133) expression level and use as a biomarker for human cancer diagnosis and therapy monitor. Blood anal. including number of circulating endothelial cells and expression levels of human genes AC133 (CD133), EST032 and U1A evaluated by NASBA anal., were determined prior to and during chemotherapy using drugs such as angiostatin or PrimMed01, gemcitabine, and cisplatin, for a wide range of human tumor types. A use of a nucleic acid mol. comprising at least part of a sequence of AC133 or an analog thereof for monitoring a treatment of an individual suffering from a disease is also provided, as well as a diagnostic kit comprising such nucleic acid mol.

IT 117570-53-3, DMXAA

RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methods of detecting CD133 antigen (AC133) expression level and use as biomarker for human cancer diagnosis and therapy monitor)

RN 117570-53-3 CAPLUS

CN 9H-Xanthene-4-acetic acid, 5,6-dimethyl-9-oxo- (9CI) (CA INDEX NAME)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2005:975665 CAPLUS Full-text

DOCUMENT NUMBER:

143:264929

TITLE:

Methods for detecting AC133 antigen mRNA for diagnosis

and treatment of cancer and other diseases

INVENTOR (S):

Penning, Maarten Tjerk; Beerepoot, Laurens Victor; Van Den Broek, Sebastiaan Johannes Jacobus; Mehra, Niven;

Voest, Emile Eugene

PATENT ASSIGNEE(S):

Primagen Holding B.V., Neth.; UMC Utrecht Holding B.V.

SOURCE:

Eur. Pat. Appl., 28 pp.

DOCUMENT TYPE:

CODEN: EPXXDW Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA	PATENT NO.					D :	DATE			APPLICATION NO.					DATE					
EP	1571		A1	-	2005	50907 EP 2004-75					686 200403									
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,			
		ΙE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL,	TR,	BG,	CZ,	EE,	HU,	PL,	SK			
CA	2558604				AA		2005	0909		CA 2005-2558604				20050302						
WO	2005083123				A1		2005	0909	1	WO 2005-NL155					20050302					
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		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	ΚŔ,	KZ,	LC,			
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		NO,	NZ,	OM,	·PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SM,			
		SY,	ТJ,	TM,	TN,	TR,	TT,	TZ,	UA,	ŪĠ,	US,	UΖ,	VC,	VN,	YU,	ZA,	ZM,	ZW		
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		RO,	SE,	SI,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,			
		MR,	ΝE,	SN,	TD,	TG														
PRIORITY	Y APP	LN.	INFO	. :]	EP 2	004-	7568	5		A 20040302					
									1	JS 2	004-	5494!	50P		P 20040302					
									1	WO 2	005-1	NL15!	5	1	W 2	0050	302			

AB The invention provides methods for detecting AC133 antigen mRNA for diagnosis and treatment of cancer and other diseases. AC133 antigen mRNA may be quantitated by PCR, RT-PCR, NASBA, SDA, TMA, bDNA or rolling circle amplification. Diseases include cancer and heart disease, high blood pressure, ischemia, stroke, psoriasis, Crohn's disease, rheumatoid arthritis, endometriosis, atherosclerosis, obesity, diabetes mellitus, diabetic retinopathy, macular degeneration, Alzheimer's disease, Peutz Jegher's syndrome, multiple sclerosis, systemic lupus erythematosus, Wegener's granulomatosis, vasculitis, sickle cell disease, thalassemia and angina.

IT 117570-53-3

> RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methods for detecting AC133 antigen mRNA for diagnosis and treatment of cancer and other diseases)

RN117570-53-3 CAPLUS

9H-Xanthene-4-acetic acid, 5,6-dimethyl-9-oxo- (9CI) (CA INDEX NAME) CN

REFERENCE COUNT:

7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 3 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN 2005:548329 CAPLUS Full-text ACCESSION NUMBER:

DOCUMENT NUMBER:

143:90113

TITLE:

Emerging drugs for ovarian cancer

AUTHOR (S):

Kelland, Lloyd R.

CORPORATE SOURCE: Antisoma Research Laboratories, St Georges Hospital

Medical School, London, SW17 0QS, UK

SOURCE: Expert Opinion on Emerging Drugs (2005), 10(2),

413-424

CODEN: EOEDA3

PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

A review. Because most patients presenting with advanced ovarian cancer are AB not curable by surgery alone, chemotherapy represents an essential component of treatment. The disease may be considered as chemosensitive, as in around three-quarters of patients major (complete) responses are seen to initial treatment with the platinum-containing drugs cisplatin and carboplatin either used alone or in combination with the taxane, paclitaxel. However, only 15 -20% of patients experience long-term remission as tumors often become resistant. The probability of achieving a second response depends on the duration of remission after first-line therapy: if this is < 6 mo (considered as platinum resistant) second responses are uncommon and usually short-lived; if this is > 6, and especially if > 12 mo (platinum sensitive), responses may be seen in about a quarter of patients, to the same drugs as used first line or to drugs such as pegylated liposomal doxorubicin, topotecan and hexamethylmelamine (all three are approved in this setting by the FDA). Gemcitabine, oral etoposide, docetaxel and oxaliplatin also show some activity either in sequential addition to existing approved of first-line therapy (as with gemcitabine) or as second-line therapy. However, there is an urgent unmet clin. need for new drugs capable of prolonging survival either by increasing long-term remission rates and/or duration as first-line treatment or to improve on outcomes of second-line treatment. Strategies currently being exploited in clin. trials include attempts to deliver more killing selectively to tumors (e.g., i.p. administration of cisplatin or radiolabeled monoclonal antibodies), agents designed to target drug resistance mechanisms (e.g., TLK-286 activated by glutathione transferase), agents targeting proteins/receptors shown to be selectively expressed in the disease (e.g., monoclonal antibodies recognizing CA-125 or HER1; small mols. targeting HER1 such as gefitinib) and disrupting established tumor vasculature (e.g., 5,6-di-Me xanthenone 4-acetic acid). At the preclin. level, agents being developed to target the phosphatidylinositol 3 kinase/AKT/mTOR pathway, and K-Ras inhibitors, may offer efficacy in the future.

IT 117570-53-3, 5,6-Dimethyl xanthenone 4-acetic acid RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(5,6-di-Me xanthenone 4-acetic acid disrupting established tumor vasculature used in treatment of ovarian cancer in patient)

RN 117570-53-3 CAPLUS

CN 9H-Xanthene-4-acetic acid, 5,6-dimethyl-9-oxo- (9CI) (CA INDEX NAME)

REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 2003:202462 CAPLUS Full-text

DOCUMENT NUMBER: 138:226761

TITLE: Synergistic anticancer combinations containing

5,6-dimethylxanthenone-4-acetic acid

INVENTOR(S): Wilson, William Robert; Siim, Bronwyn Gae

PATENT ASSIGNEE(S): Cancer Research Technology Limited, UK

PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

SOURCE:

Patent English

LANGUAGE:

COINTE, 1

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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WO	O 2003020259			A3 20030417															
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		CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR	, NE,	SN,	TD,	TG					
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EP	1423	105			A2	A2 20040602			EP 2002-758562						20020903				
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NZ	5310	45			Α	A 20060831			NZ 2002-531045					20020903					
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AB The present invention relates to synergistic combinations of the 5,6dimethylxanthenone-4-acetic acid (DMXAA) and a compound selected from platinum compds., Vinca alkaloids, alkylating agents, anthracyclines, topoisomerase I inhibitors, antimetabolites and topoisomerase II inhibitors, which have antitumor activity. More particularly, the invention is concerned with the use of such combinations in the treatment of cancer and pharmaceutical compds. containing the combinations. The antitumor activity and host toxicity of DMXAA/cytotoxic drug combinations was assessed by varying the dose of chemotherapeutic drug up to the toxicity limit, with co-administration of a fixed DMXAA dose (80 µmol/kg, ca. 80% of MTD), and evaluating subsequent tumor growth delay. Of the 7 drugs investigated, 4 (doxorubicin, 5-fluorouracil, cyclophosphamide and cisplatin) had appreciable activity against this tumor as indicated by dose-response relationships providing significant slopes by linear regression, and highly significant growth delays of 10 days at their MTDs.

IT 117570-53-3, 5,6-Dimethylxanthenone-4-acetic acid
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(synergistic anticancer combinations containing dimethylxanthenoneacetic acid)

ANSWER 5 OF 7 USPATFULL on STN

ACCESSION NUMBER:

2005:240102 USPATFULL Full-text

CN

Hydrogels used to deliver medicaments to the eye for

the treatment of posterior segment diseases

INVENTOR(S):

Schultz, Clyde L., Ponte Vedra, FL, UNITED STATES

NUMBER KIND DATE ------US 2005208102 A1 20050922

PATENT INFORMATION:

APPLICATION INFO.: US 2004-821718 A1 20040409 (10)

> NUMBER DATE -----

PRIORITY INFORMATION:

US 2003-461354P 20030409 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

FINCH IP LLC, P.O. BOX 1358, CONCORD, NH, 03302, US LEGAL REPRESENTATIVE:

NUMBER OF CLAIMS: 20

EXEMPLARY CLAIM: 1 LINE COUNT: 502

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a polymeric drug delivery system including a hydrogel containing one or more drugs for the treatment of a posterior segment disease. Allowing passive transference of this drug from a dilute solution into the hydrogel produces the delivery system. The hydrogel, when placed in contact with the eye, delivers the drug. The delivery of the drug is sustained over an extended period of time, which is of particular utility in the eye, which is periodically flushed with tears. This sustained delivery accelerates the treatment process while avoiding potential damaging effects of localized delivery of high concentrations of compounds, e.g., from eye drops.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 117570-53-3, DMXAA

(hydrogels containing drugs for treatment of eye diseases in posterior segment)

RN 117570-53-3 USPATFULL

9H-Xanthene-4-acetic acid, 5,6-dimethyl-9-oxo- (9CI) (CA INDEX NAME) CN

L5 ANSWER 6 OF 7 USPATFULL on STN

ACCESSION NUMBER: 2005:87035 USPATFULL Full-text

Telephone in the second second

TITLE: Hydrogels used to deliver medicaments to the eye for

the treatment of posterior segment diseases

INVENTOR(S): Schultz, Clyde L., Ponte Vedra, FL, UNITED STATES

APPLICATION INFO.: US 2004-971997 A1 20041022 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2004-821718, filed

on 9 Apr 2004, PENDING

. NUMBER DATE

PRIORITY INFORMATION: US 2003-461354P 20030409 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: CLARK & ELBING LLP, 101 FEDERAL STREET, BOSTON, MA,

02110

NUMBER OF CLAIMS: 27
EXEMPLARY CLAIM: 1
LINE COUNT: 582

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

This invention provides a polymeric drug delivery system including a hydrogel containing one or more drugs for the treatment of a posterior segment disease. Exemplary drugs are anti-angiogenesis compounds for the treatment of macular degeneration. Allowing passive transference of this drug from a dilute solution into the hydrogel produces the delivery system. The hydrogel, when placed in contact with the eye, delivers the drug. The delivery of the drug is sustained over an extended period of time, which is of particular utility in the eye, which is periodically flushed with tears. This sustained delivery accelerates the treatment process while avoiding potential damaging effects of localized delivery of high concentrations of compounds, e.g., from eye drops.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 117570-53-3, DMXAA

(hydrogels containing drugs for treatment of eye diseases in posterior segment)

RN 117570-53-3 USPATFULL

CN 9H-Xanthene-4-acetic acid, 5,6-dimethyl-9-oxo- (9CI) (CA INDEX NAME)

L5 ANSWER 7 OF 7 USPATFULL on STN

ACCESSION NUMBER: 2004:261978 USPATFULL Full-text

TITLE: Anti-cancer combinations

INVENTOR(S): Wilson, William R., Waiuku, NEW ZEALAND

Siim, Bronwyn G., Mt. Eden, NEW ZEALAND

PATENT ASSIGNEE(S): Cancer Research Technology Limited (non-U.S.

corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 2004204480 Al 20041014

APPLICATION INFO.: US 2004-790943 A1 20040302 (10)

NUMBER DATE

PRIORITY INFORMATION: WO 2002-GB4025 20020903

GB 2001-21285 20010903

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: PALMER & DODGE, LLP, KATHLEEN M. WILLIAMS; 111

HUNTINGTON AVENUE, BOSTON, MA, 02199

NUMBER OF CLAIMS: 23 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 2 Drawing Page(s)

LINE COUNT: 1297

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention relates to synergistic combinations of the compound 5,6-dimethylxanthenone-4-acetic acid (DMXAA) and a compound selected from platinum compounds, vinca alkaloids, alkylating agents, anthracyclines, topoisomerase I inhibitors, antimetabolites and topoisomerase II inhibitors, which have anti-tumour activity. Preferably, the present invention relates to synergistic combinations of the compound 5,6-dimethylxanthenone-4-acetic acid (DMXAA) and a compound selected from carboplatin, gemcitabine, cisplatin, 5-fluorouracil, cyclophosphamide, etoposide, vincristine, doxorubicin and irinotecan. More particularly, the invention is concerned with the use of such combinations in the treatment of cancer and pharmaceutical compositions containing such combinations. The invention further provides for methods of preparing the combinations of the invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 117570-53-3, 5,6-Dimethylxanthenone-4-acetic acid

(synergistic anticancer combinations containing dimethylxanthenoneacetic acid)

RN 117570-53-3 USPATFULL

CN 9H-Xanthene-4-acetic acid, 5,6-dimethyl-9-oxo- (9CI) (CA INDEX NAME)

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FILE 'REGISTRY' ENTERED AT 09:28:56 ON 08 NOV 2006

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L3 1 S L1 EXA FULL

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L4

280 S L3

L5 7 S L4 AND "GEMCITABINE"

=> s 14 and "combined chemotherapy"

L6 8 L4 AND "COMBINED CHEMOTHERAPY"

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L6 ANSWER 1 OF 8 MEDLINE on STN

ACCESSION NUMBER: 2002733282 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 12497205

TITLE: Marked potentiation of the antitumour activity of

chemotherapeutic drugs by the antivascular agent

5,6-dimethylxanthenone-4-acetic acid (DMXAA).

AUTHOR: Siim Bronwyn G; Lee Alan E; Shalal-Zwain Sahar; Pruijn

Frederik B; McKeage Mark J; Wilson William R

CORPORATE SOURCE: Molecular Medicine and Pathology, The University of

Auckland, Private Bag 92019, Auckland, New Zealand.

SOURCE: Cancer chemotherapy and pharmacology, (2003 Jan) Vol. 51,

No. 1, pp. 43-52. Electronic Publication: 2002-11-12.

Journal code: 7806519. ISSN: 0344-5704.

PUB. COUNTRY: Germany: Germany, Federal Republic of DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200302

ENTRY DATE: Entered STN: 27 Dec 2002

Last Updated on STN: 26 Feb 2003 Entered Medline: 25 Feb 2003

PURPOSE. To determine whether there is a therapeutic interaction between the antivascular agent 5,6-dimethylxanthenone-4-acetic acid (DMXAA) and nine chemotherapy drugs against an early-passage mouse mammary tumour (MDAH-MCa-4), and to investigate the mechanism of any such interaction. METHODS AND RESULTS. Female C3H/HeN mice bearing intramuscular MDAH-MCa-4 tumours were injected intraperitoneally with DMXAA (80 micro mol/kg) or chemotherapy drug (at a range up to the maximum tolerated dose) alone, or coadministered. A small reduction in the dose of the chemotherapy drug was required in most cases, but the increase in antitumour effect was much greater than the increase in host toxicity (body weight loss). The therapeutic gain increased in the order 5-fluorouracil (no gain)<(etoposide, carboplatin, cyclophosphamide, doxorubicin,

cisplatin) < (docetaxel, vincristine) < paclitaxel. The interaction with paclitaxel (31.6 micro mol/kg) was striking, with coadministration of DMXAA extending the median tumour growth delay from 0.3 to 80 days with three of seven animals cured. The interaction showed a broad timing of the optimum with similar activity when paclitaxel was administered 4 h before to 1 h after DMXAA. No therapeutic synergy was obtained when paclitaxel was combined with the antivascular agent combretastatin A4 phosphate (227 micro mol/kg), which induced only transient blood flow inhibition in this tumour, measured using the H33342 perfusion marker. Paclitaxel did not enhance the antivascular activity of DMXAA. Plasma and tumour concentrations of paclitaxel (and carboplatin), measured by LC-MS and ICP-MS respectively, were not elevated by combination with DMXAA. CONCLUSIONS. There was a dramatic therapeutic interaction between DMXAA and standard chemotherapy drugs, particularly paclitaxel, against the MDAH-MCa-4 tumour, which was not due to a pharmacokinetic interaction or potentiation of antivascular activity. It is suggested that the major mechanism of synergy is killing of cells by DMXAA in poorly perfused regions of tumours that are inaccessible to chemotherapy drugs.

L6 ANSWER 2 OF 8 MEDLINE on STN

ACCESSION NUMBER: 2002625620 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 12382527

TITLE: Potential of DMXAA combination therapy for solid tumors.

AUTHOR: Baguley Bruce C; Wilson William R

CORPORATE SOURCE: Auckland Cancer Society Research Centre, University of

Auckland, Auckland, New Zealand. b.baguley@auckland.ac.nz

SOURCE: Expert review of anticancer therapy, (2002 Oct) Vol. 2, No.

5, pp. 593-603. Ref: 84

Journal code: 101123358. ISSN: 1473-7140.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200308

ENTRY DATE: Entered STN: 18 Oct 2002

Last Updated on STN: 28 Aug 2003 Entered Medline: 27 Aug 2003

AB DMXAA is one of the first examples of a new class of anticancer agents that attack existing tumor blood vessels and thus deprives tumor tissue of an adequate blood supply. Its mechanism of action appears to rely on the induction within tumor tissue of cytokines, such as tumor necrosis factor. In experimental tumors, DMXAA interacts productively with radiation, hyperthermia and a number of chemotherapeutic drugs. This review discusses the mechanisms underlying such interactions and how these might be exploited in clinical cancer treatment.

L6 ANSWER 3 OF 8 MEDLINE on STN

ACCESSION NUMBER: 2002211409 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 11948484

TITLE: Vascular targeting agents enhance chemotherapeutic agent

activities in solid tumor therapy.

AUTHOR: Siemann Dietmar W; Mercer Emma; Lepler Sharon; Rojiani Amyn

М

CORPORATE SOURCE: Department of Radiation Oncology, Shands Cancer Center,

University of Florida, Gainesville, FL 32610, USA..

siemadw@ufl.edu

CONTRACT NUMBER: CA84408 (NCI)

SOURCE: International journal of cancer. Journal international du

cancer, (2002 May 1) Vol. 99, No. 1, pp. 1-6.

Journal code: 0042124. ISSN: 0020-7136.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200205

ENTRY DATE: Entered STN: 12 Apr 2002

Last Updated on STN: 2 May 2002 Entered Medline: 1 May 2002

The utility of combining the vascular targeting agents 5,6-dimethyl-AB xanthenone-4 acetic acid (DMXAA) and combretastatin A-4 disodium phosphate (CA4DP) with the anticancer drugs cisplatin and cyclophosphamide (CP) was evaluated in experimental rodent (KHT sarcoma), human breast (SKBR3) and ovarian (OW-1) tumor models. Doses of the vascular targeting agents that led to rapid vascular shutdown and subsequent extensive central tumor necrosis were identified. Histologic evaluation showed morphologic damage of tumor cells within a few hours after treatment, followed by extensive hemorrhagic necrosis and dose-dependent neoplastic cell death as a result of prolonged ischemia. Whereas these effects were induced by a range of CA4DP doses (10-150 mg/kg), the dose response to DMXAA was extremely steep; doses < or = 15 mg/kg were ineffective and doses > or = 20 mg/kg were toxic. DMXAA also enhanced the tumor cell killing of cisplatin, but doses > 15 mg/kg were required. contrast, CA4DP increased cisplatin-induced tumor cell killing at all doses studied. This enhancement of cisplatin efficacy was dependent on the sequence and interval between the agents. The greatest effects were achieved when the vascular targeting agents were administered 1-3 hr after cisplatin. When CA4DP (100 mg/kg) or DMXAA (17.5 mg/kg) were administered 1 hr after a range of doses of cisplatin or CP, the tumor cell kill was 10-500-fold greater than that seen with chemotherapy alone. In addition, the inclusion of the antivascular agents did not increase bone marrow stem cell toxicity associated with these anticancer drugs, thus giving rise to a therapeutic gain. Copyright 2002 Wiley-Liss, Inc.

L6 ANSWER 4 OF 8 MEDLINE on STN

ACCESSION NUMBER: 2002135262 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 11870905

TITLE: Differential sensitivity of two adenocarcinoma xenografts

to the anti-vascular drugs combretastatin A4 phosphate and 5,6-dimethylxanthenone-4-acetic acid, assessed using MRI

and MRS.

AUTHOR: Beauregard Daniel A; Pedley R Barbara; Hill Sally A;

Brindle Kevin M

CORPORATE SOURCE: Department of Biochemistry, University of Cambridge,

Cambridge CB2 1GA, UK.

SOURCE: NMR in biomedicine, (2002 Apr) Vol. 15, No. 2, pp. 99-105.

Journal code: 8915233. ISSN: 0952-3480.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200206

ENTRY DATE: Entered STN: 1 Mar 2002

Last Updated on STN: 21 Jun 2002 Entered Medline: 20 Jun 2002

AB The effects of two anti-vascular agents, combretastatin A4 phosphate (CA4P), and 5,6-dimethylxanthenone-4-acetic acid (DMXAA), on the perfusion of two human colon adenocarcinomas implanted in SCID mice, were assessed for up to 3

h using non-invasive magnetic resonance imaging (MRI) and spectroscopy techniques (MRS). MRI measurements of GdDTPA inflow showed that treatment with CA4P had little effect on the perfusion of HT29 tumours. Localized (31)P MRS measurements also showed that the drug had no significant effect on tumour cell energy status, as assessed from the ratio of the integrals of the signals from inorganic phosphate (P(i)) and nucleoside triphosphates. However, after treatment with DMXAA, perfusion was reduced and the P(i)/NTP ratio increased, indicating that the HT29 tumour is susceptible to the action of this drug. The LS174T tumour model was susceptible to both CA4P and DMXAA, using the criteria of changes in GdDTPA inflow and P(i)/NTP ratio. Copyright 2002 John Wiley & Sons, Ltd.

L6 ANSWER 5 OF 8 MEDLINE on STN

ACCESSION NUMBER: 2002133988 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 11868972

TITLE: Species differences in the metabolism of the antitumour

agent 5,6-dimethylxanthenone-4-acetic acid in vitro: implications for prediction of metabolic interactions in

vivo.

AUTHOR: Zhou S F; Tingle M D; Kestell P; Paxton J W

CORPORATE SOURCE: Division of Pharmacology and Clinical Pharmacology, Faculty

of Medical and Health Sciences, University of Auckland, New

Zealand.. shufeng.zhou@auckland.ac.nz

SOURCE: Xenobiotica; the fate of foreign compounds in biological

systems, (2002 Feb) Vol. 32, No. 2, pp. 87-107.

Journal code: 1306665. ISSN: 0049-8254.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200209

ENTRY DATE: Entered STN: 1 Mar 2002

Last Updated on STN: 6 Sep 2002 Entered Medline: 4 Sep 2002

AB Mouse studies have indicated that the antitumour effects of 5,6dimethylxanthenone-4-acetic acid (DMXAA) are dramatically potentiated in combination with other drugs, and it has been proposed that optimization of the therapeutic potential of DMXAA would exploit combination therapy. The aim was to identify the most appropriate animal model for further investigations of the pharmacokinetics of possible DMXAA-drug combinations and their extrapolation to patients. 2. Qualitatively, the metabolic profile for DMXAA in liver microsomes was similar in mouse, rat, rabbit and humans, with glucuronidation and 6-methylhydroxylation the two major metabolic pathways. In all species, the intrinsic clearance by glucuronidation was at least 2-fold that due to hydroxylation. There was significant variability in the in vitro kinetic parameters (Km, Vmax), with the mouse being the least efficient DMXAA metabolizer compared with the other species. 3. Mouse, rat and rabbit renal microsomes exhibited DMXAA glucuronidation activity, but only the rabbit showed 6-methylhydroxylation. For the total in vitro CL(int) (Vmax/Km) by glucuronidation and 6-methylhydroxylation, the ratio of kidney:liver was 0.67, 0.03 and 0.34 in the mouse, rat and rabbit respectively. However, taking into account the liver and kidney weight difference, it is apparent that the in vivo renal metabolism would not be a major contributor to the overall elimination of DMXAA. 4. The inhibitory profile for liver DMXAA glucuronidation was similar across species, but there was remarkable interspecies variability in the inhibition of liver DMXAA 6methylhydroxylation. 5. Extrapolation of in vitro intrinsic clearance to in vivo gave a significant underestimation of plasma clearance for all species. However, there was a significant allometric relationship for plasma clearance

and volume of distribution, but not for maximum tolerated dose across species. 6. The results indicate that animal models may have a limited role in the extrapolation to patients of drug interactions with agents such as DMXAA that have immunomodulating activity that may vary widely between species.

L6 ANSWER 6 OF 8 MEDLINE on STN

ACCESSION NUMBER: 2001189654 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 11280751

TITLE: Vascular attack by 5,6-dimethylxanthenone-4-acetic acid

combined with B7.1 (CD80)-mediated immunotherapy overcomes immune resistance and leads to the eradication of large

tumors and multiple tumor foci.

AUTHOR: Kanwar J R; Kanwar R K; Pandey S; Ching L M; Krissansen G W

CORPORATE SOURCE: Department of Molecular Medicine, School of Medicine and

Health Science, University of Auckland, New Zealand.

SOURCE: Cancer research, (2001 Mar 1) Vol. 61, No. 5, pp. 1948-56.

Journal code: 2984705R. ISSN: 0008-5472.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200104

ENTRY DATE: Entered STN: 25 Apr 2001

Last Updated on STN: 25 Apr 2001 Entered Medline: 19 Apr 2001

AB The promise of cancer immunotherapy is that it will not only eradicate primary tumors but will generate systemic antitumor immunity capable of destroying distant metastases. A major problem that must first be surmounted relates to the immune resistance of large tumors. Here we reveal that immune resistance can be overcome by combining immunotherapy with a concerted attack on the tumor vasculature. The functionally related antitumor drugs 5,6dimethylxanthenone-4-acetic acid (DMXAA) and flavone acetic acid (FAA), which cause tumor vasculature collapse and tumor necrosis, were used to attack the tumor vasculature, whereas the T-cell costimulator B7.1 (CD80), which costimulates T-cell proliferation via the CD28 pathway, was used to stimulate antitumor immunity. The injection of cDNA (60-180 microg) encoding B7.1 into large EL-4 tumors (0.8 cm in diameter) established in C57BL/6 mice, followed 24 h later by i.p. administration of either DMXAA (25 mg/kg) or FAA (300 mg/kg), resulted in complete tumor eradication within 2-6 weeks. monotherapies were ineffective. Both vascular attack and B7.1 immunotherapy led to up-regulation of heat shock protein 70 on stressed and dying tumor cells, potentially augmenting immunotherapy. Remarkably, large tumors took on the appearance of a wound that rapidly ameliorated, leaving perfectly healed skin. Combined therapy was mediated by CD8+ T cells and natural killer cells, accompanied by heightened and prolonged antitumor cytolytic activity (P < 0.001), and by a marked increase in tumor cell apoptosis. Cured animals completely rejected a challenge of 1 x 10(7) parental EL-4 tumor cells but not a challenge of 1 x 10(4) Lewis lung carcinoma cells, demonstrating that antitumor immunity was tumor specific. Adoptive transfer of 2 x 10(8) splenocytes from treated mice into recipients bearing established (0.8 cm in diameter) tumors resulted in rapid and complete tumor rejection within 3 weeks. Although DMXAA and B7.1 monotherapies are complicated by a narrow range of effective doses, combined therapy was less dosage dependent. Thus, a broad range of amounts of B7.1 cDNA were effective in combination with 25 mg/kg DMXAA. In contrast, DMXAA, which has a very narrow range of high active doses, was effective at a low dose (18 mg/kg) when administered with a large amount (180 microg) of B7.1 cDNA. Importantly, combinational therapy generated heightened antitumor immunity, such that gene transfer of B7.1 into one tumor, followed by systemic DMXAA treatment, led to the complete rejection

of multiple untreated tumor nodules established in the opposing flank. These findings have important implications for the future direction and utility of cancer immunotherapies aimed at harnessing patients' immune responses to their own tumors.

L6 ANSWER 7 OF 8 MEDLINE on STN

ACCESSION NUMBER: 1999287394 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 10360649

TITLE: Thalidomide increases both intra-tumoural tumour necrosis

factor-alpha production and anti-tumour activity in response to 5,6-dimethylxanthenone-4-acetic acid.

AUTHOR: Cao Z; Joseph W R; Browne W L; Mountjoy K G; Palmer B D;

Baguley B C; Ching L M

CORPORATE SOURCE: Auckland Cancer Society Research Centre, University of

Auckland School of Medicine, New Zealand.

SOURCE: British journal of cancer, (1999 May) Vol. 80, No. 5-6, pp.

716-23.

Journal code: 0370635. ISSN: 0007-0920.

PUB. COUNTRY: SCOTLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; AIDS

ENTRY MONTH: 199906

ENTRY DATE: Entered STN: 12 Jul 1999

Last Updated on STN: 12 Jul 1999 Entered Medline: 23 Jun 1999

AB 5,6-Dimethylxanthenone-4-acetic acid (DMXAA), synthesized in this laboratory and currently in phase I clinical trial, is a low molecular weight inducer of tumour necrosis factor-alpha (TNF-alpha). Administration of DMXAA to mice with established transplantable tumours elicits rapid vascular collapse selectively in the tumour, followed by extensive haemorrhagic necrosis mediated primarily through the production of TNF-alpha. In this report we have investigated the synthesis of TNF-alpha mRNA in hepatic, splenic and tumour tissue. Coadministration of thalidomide with DMXAA increased anti-tumour activity and increased intra-tumoural TNF-alpha production approximately tenfold over that obtained with DMXAA alone. Thalidomide increased splenic TNF-alpha production slightly but significantly decreased serum and hepatic levels of TNF-alpha induced with DMXAA. Lipopolysaccharide (LPS) induced 300-fold higher serum TNF-alpha than did DMXAA at the maximum tolerated dose, but induced similar amounts of TNF-alpha in spleen, liver and tumour. Splenic TNF-alpha activity induced with LPS was slightly increased with thalidomide, but serum and liver TNF-alpha levels were suppressed. Thalidomide did not increase intra-tumoural TNF-alpha production induced with LPS, in sharp contrast to that obtained with DMXAA. While thalidomide improved the anti-tumour response to DMXAA, it had no effect on the anti-tumour action of LPS that did not induce a significant growth delay or cures against the Colon 38 tumour. The increase in the antitumour action by thalidomide in combination with DMXAA corresponded to an increase in intra-tumoural TNF-alpha production. Co-administration of thalidomide may represent a novel approach to improving selective intratumoural TNF-alpha production and anti-tumour efficacy of DMXAA.

L6 ANSWER 8 OF 8 MEDLINE on STN

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agent 5,6-dimethylxanthenone-4-acetic acid (DMXAA) by combination with 5-hydroxytryptamine and bioreductive

drugs.

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AB The tumour blood flow inhibitor 5,6-dimethylxanthenone-4-acetic acid (DMXAA) causes dramatic haemorrhagic necrosis in murine tumours, but activity is seen only at doses close to the toxic limit. This study investigates two approaches for increasing the therapeutic ratio of DMXAA. The first approach combines DMXAA with a second tumour blood flow inhibitor, 5-hydroxytryptamine (5-HT). Co-administration of 5-HT (700 micromol kg(-1)) to C3H mice caused marked enhancement of DMXAA effects against MDAH-MCa-4 tumours, with dosemodifying factors (DMFs) of >3 for blood flow inhibition (at 4 h), 2.3 for necrosis (at 12 h) and 2.0 for growth delay, without compromising the maximum tolerated dose of DMXAA (90 micromol kg(-1)). The data are consistent with ischaemic injury to the tumour being the major mechanism of anti-tumour activity. The second approach combines DMXAA (+/- 5-HT) with hypoxiaselective bioreductive drugs. Anti-tumour activity of all three bioreductive drugs tested (tirapazamine, CI-1010, SN 23816) was strongly potentiated by DMXAA, suggesting that there is a population of reversibly hypoxic tumour cells after DMXAA treatment. Co-administration of 5-HT further potentiated anti-tumour activity, but also increased host toxicity of tirapazamine and CI-1010 so that little therapeutic benefit was achieved. In contrast, the host toxicity of the dinitrobenzamide mustard SN 23816 was only slightly increased by DMXAA/5-HT, whereas the tumour growth delay at the maximum tolerated dose of SN 23816 was increased from 3.5 to 26.5 days. This study demonstrates that 5-HT and/or bioreductive drugs can improve the therapeutic activity of DMXAA in mice, and that with SN 23816 both approaches can be used together to provide considerably enhanced anti-tumour activity.

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(FILE 'HOME' ENTERED AT 09:28:31 ON 08 NOV 2006)

FILE 'REGISTRY' ENTERED AT 09:28:56 ON 08 NOV 2006

L1 STRUCTURE UPLOADED

L2 0 S L1

L3 1 S L1 EXA FULL

FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 09:29:39 ON 08 NOV 2006

L4 280 S L3

L5 7 S L4 AND "GEMCITABINE"

L6 8 S L4 AND "COMBINED CHEMOTHERAPY"

---Logging off of STN---